reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed had possession of the claimed invention.

According to the Examiner, the specification does not provide sufficient written description to support the genus of fragments of SEQ ID NO:1 as encompassed by the rejected claims. Applicants respectfully traverse the rejection for the reasons set forth below.

The specification teaches that a fragment is a nucleic acid consisting of contiguous nucleotides derived from SEQ ID NO:1 (as claimed). These fragments range in size, and may be as short as 8 nucleotides, or as long as 2946 nucleotides (i.e., full length minus 8 nucleotides). The specification further teaches that the fragment can begin at the first nucleotide, the second nucleotide, the third nucleotide, etc. of SEQ ID NO:1, and respectively end at the eighth nucleotide, the ninth nucleotide, the tenth nucleotide, etc. of SEQ ID NO:1. The specification further teaches:

> " ... this disclosure intends to embrace each and every fragment of each sequence, beginning at the first nucleotide, the second nucleotide and so on, up to 8 nucleotides short of the end, and ending anywhere from nucleotide number 8, 9, 10 and so on for each sequence, up to the very last nucleotide, provided the sequence is unique as described above. Taking into account the exclusion described above, virtually any segment of the region of SEQ ID NO:1 beginning at nucleotide 1 and ending at nucleotide 2954, ... or complements thereof, that is 20 or more nucleotides in length will be unique. Those skilled in the art are well versed in methods for selecting such sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from other sequences in the human genome of the fragment to those on known databases typically is all that is necessary, although *in vitro* confirmatory hybridization and sequencing analysis may be performed." (See, page 25, lines 2-15.)

SEQ ID NO:1 has the following sequence:

```
cgctgtttgt ccagcttctc agagttgctg tgcagctcgg atgtggcata ggaaacagca     60
gacacaggga gagggcagca taaggcactg tagggagcag tggccacatt ttctgcagag    120
gaagaaccg atg ctg gaa cgt cgt tgc agg ggc ccc ctg gcc atg ggc ctg    171
gcc cag ccc cga ctc ctt tct ggg ccc tcc cag gag tca ccc cag acc      219
ctg ggg aag gag tcc cgc ggg ctg agg caa caa ggc acg tca gtg gcc      267
cag tct ggt gcc caa gcc cca ggc agg gcc cat cgc tgt gcc cac tgt      315
cga agg cac ttc cct ggc tgg gtg gct ctg tgg ctt cac acc cgc cgg      363
tgc cag gcc cgg ctg ccc ttg ccc tgc cct gag tgt ggc cgt cgc ttt      411
cgc cat gcc ccc ttc tta gca ctg cac cgc cag gtc cat gct gct gcc      459
acc cca gac ctg ggc ttt gcc tgc cac ctc tgt ggg cag agc ttc cga      507
ggc tgg gtg gcc ctg gtt ctg cat ctg ctg gcc cat tca gct gca aag      555
caa ccc atc gct tgt ccc aaa tgc gag aga cgc ttc tgg cga cga aag      603
cag ctt cga gct cat ctg cgg cgg tgc cac cct ccc gcc ccg gag gcc      651
cgg ccc ttc ata tgc ggc aac tgt ggc cgg agc ttt gcc cag tgg gac      699
cag cta gtt gcc cac aag cgg gtg cac gta gct gag gcc ctg gag gag      747
gcc gca gcc aag gct ctg ggg ccc cgg ccc agg ggc cgc ccc gcg gtg      795
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acc gcc ccc cgg ccc ggt gga gat gcc gtc gac cgc ccc ttc cag tgt      843
gcc tgt tgt ggc aag cgc ttc cgg cac aag ccc aac ttg atc gct cac      891
cgc cgc gtg cac acg ggc gag cgg ccc cac cag tgc ccc gag tgc ggg      939
aag cgc ttt acc aat aag ccc tat ctg act tcg cac cgg cgc atc cac      987
acc ggc gag aag ccc tac ccg tgc aaa gag tgc ggc cgc cgc ttc cgg     1035
cac aaa ccc aac ctg ctg tct cac agc aag att cac aag cga tcc gag     1083
ggg tcg gcc cag gcc gcc ccc ggc ccg ggg agc ccc cag ctg cca gcc     1131
ggc ccc cag gag tcc gcg gcc gag ccc acc ccg gcg gta cct ctg aaa     1179
ccg gcc cag gag ccg ccg cca ggg gcc ccg cca gag cac ccg cag gac     1227
ccg atc gaa gcc ccc ccc tcc ctc tac agc tgc gac gac tgc ggc agg     1275
agc ttc cgg ctg gag cgc ttc ctg cgg gcc cac cag cgg cac gac acc     1323
ggg gag cgg ccc ttc acc tgc gcc gag tgc ggg aag aac ttc ggc aag     1371
aag acg cac ctg gtg gcg cac tcg ccg gtg cac tcc ggc gag cgg ccc     1419
ttc gcc tgc gag gag tgc ggc cgc cgc ttc tcc cag ggc agc cat ctg     1467
gcg gcg cat cgg ccg gac cac gcc ccc gat cgg ccc ttc gtg tgt ccc     1515
gac tgc ggc aag gcc ttc cgc cac aaa ccc tac ctg gcg cgg cac cgg     1563
cgc atc cac acc ggc gag aag ccc tac gtc tgc ccc gac tgc ggc aaa     1611
gcc ttc agc cag aag tcc aac ctg gtg tcg cac cgg cgc atc cac acg     1659
ggc gag cgg ccc tac gcc tgt ccc gac tgc gac cgc agc ttc agc cag     1707
aag tcc aac ctc atc acc cac cgc aag agc cac atc cgg gac ggc gcc     1755
ttc tgc tgt gcc atc tgt ggc cag acc ttc gac gac gag gag aga ctc     1803
ctg gcc cac cag aag aag cac gat gtc t gagacggtgg gcggggccgt         1851
gttggctgag agagggctgg ggtccttcgt ggtgggagtc gcagtgggct gggggtgcct   1911
gcctagtgct ggagtagggg acaatgggaa tcctagaggg gatggaagat gcggggagtg   1971
agctgggtgg gccctgctag cgagagaggt caaccccggt ggccagggaa cccacttcca   2031
agcgcaggga cgccggcctc cagctggtgt gtgctaaggc tccgtcctga ctgccctgtg   2091
ccctggaaaa gcagcaatac atccgccccc tacagccctc tggctagagg agccaccagt   2151
ggaaaggaag ccctccatcc tctggtatta acgccttaat gcccctgtct tttactgtaa   2211
gttacttaga tcatttttgg aagcaggcgt ggtagagtcc tgtaaatgaa tgctctgggc   2271
tagatacagc ttggagaacc tgctggcctt gttagacaga acttgggcct ttgccagcag   2331
caagaggtga agcgaagcca ctcttacctc tcccttcccc tcccacctgc cccctgcgta   2391
ggcacccaga cttggagaga cccgtctgct gttaatactt ccatcctctt ccttcccaaa   2451
gagcagatcc caaggcattt actccttggt ctgtctcgct ttatctgtcg cccctcccag   2511
cgctgagagc ctcccctggc tgtcagcagc actgtgtcca ggctcttgtc tgaacaccgc   2571
agcccctcct tcgctccttc cacagctcag catgtcacgg caaggactgc cgcattggtg   2631
atggagggcc agctgagggg aagttgctgg tgagtttcct ttctccattt ctagcatatg   2691
acacctggcc tctgcttgag cacttaggtg acaggaactt ccgcacctcc tgaggccctg   2751
gatgattcta attgttagaa attctaattg ttagaaatcc ttccttataa tgaatgaatt   2811
ctgctttcct ataatttcta cctattgggc cttgttctgt tctctggaac taaacagaac   2871
aaccatttac ccctcctttt caaactagag aataaacatt tggttttaga aaaaaaaaaa   2931
aaaaaaaaaa aaaaaaaaaa aaa                                           2954
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Accordingly, one or ordinary skill knowing the sequence of SEQ ID NO:1 and following the teachings of the specification can readily compile a list of fragments that include but are not limited to: CGCTGTTT (nucleotides 1-8); CGCTGTTTG (nucleotides 1-9); CGCTGTTTGT (nucleotides 1-10); CGCTGTTTGTC (nucleotides 1-11); CGCTGTTTGTCC (nucleotides 1-12); CGCTGTTTGTCCA (nucleotides 1-13); CGCTGTTTGTCCAG (nucleotides 1-14); CGCTGTTTGTCCAGC (nucleotides 1-15); CGCTGTTTGTCCAGCT (nucleotides 1-16); CGCTGTTTGTCCAGCTT (nucleotides 1-17); CGCTGTTTGTCCAGCTTC (nucleotides 1-

18); CGCTGTTTGTCCAGCTTCT (nucleotides 1-19); CGCTGTTTGTCCAGCTTCTC (nucleotides 1-20); CGCTGTTTGTCCAGCTTCTCA (nucleotides 1-21); CGCTGTTTGTCCAGCTTCTCAG (nucleotides 1-22); CGCTGTTTGTCCAGCTTCTCAGA (nucleotides 1-23); CGCTGTTTGTCCAGCTTCTCAGAG (nucleotides 1-24); etc.

One of ordinary skill will also readily appreciate that a more expeditious manner of identifying fragments of SEQ ID NO:1 that are novel over the prior art involves comparing SEQ ID NO:1 to a database of known sequences (e.g., GenBank), using an appropriate program (e.g., BLAST). The results of such a comparison will immediately identify fragments of SEQ ID NO:1 that are in the prior art, and thus not embraced by the pending claims. The Examiner has presumably already conducted such a search as evidenced by the outstanding prior art rejections, thus no other searching is required on the part of the Examiner.

In view of foregoing, Applicants respectfully request that the Examiner reconsider and withdraw his rejection of claims 6 and 8-10 under 35 U.S.C. §112, first paragraph, written description.

Enablement:

The Examiner has rejected claims 6 and 8-10 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a nucleic acid comprising SEQ ID NO:1, does not reasonably provide enablement fro nucleic acids comprising fragments of SEQ ID NO:1. The Examiner states that the specification is silent on the use of said fragments, and on what properties said fragments need to possess in order to be used and how said fragments are to be used. Applicants respectfully traverse the rejection for the reasons set forth below.

Applicants refer the Examiner to page 25, lines 11-15 of the specification which states that

> "Those skilled in the art are well versed in methods for selecting such sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from other sequences in the human genome of the fragment to those on known databases typically is all that is necessary, although *in vitro* confirmatory hybridization and sequencing analysis may be performed."

As discussed above (see Written Description), one of ordinary skill in the art can identify fragments of SEQ ID NO:1 based on the sequence of SEQ ID NO:1, and can readily determine whether such sequences are in the prior art. Such an analysis does not involve undue experimentation. Rather, this is the quality of experimentation that one of ordinary skill in the

art routinely engages in in order to determine the origin and "uniqueness" of a nucleic acid sequence of interest. With respect to the use of such fragments, the specification explicitly teaches that the fragments can be used as probes in Southern and Northern blot assays, or as primers for PCR reactions. (See page 24, lines 19-21.) The fragments can also be used as antisense molecules to inhibit RIP60 expression. (See page 24, lines 27-29.) With respect to the length of such fragments, claim 6 has been amended to recite that the fragment is at least 8 nucleotides in length.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw his rejection of now pending claims 6 and 8-10 under 35 U.S.C. §112, first paragraph, enablement.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 1-6 and 8-16 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner has rejected claim 1 as vague and indefinite due to the recitation of an improper Markush group. Applicants have amended claim 1. Claim 1 should now be considered definite.

The Examiner has rejected claims 6 and 9 as vague and indefinite due to the recitation of the term "fragment" and the unknown lower limit of that term. Claim 6 has been amended to recite that the fragment is at least 8 nucleotides in length. Claims and 9 should now be considered definite.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-6 and 8-16 under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102(a)

The Examiner has maintained his rejection of claims 1-3, 6 and 8-9 under 35 U.S.C. §102(a) in view of Sulston et al. (Genome Research, 8(11):1097-1108, 1998), for the reasons of record.

Applicants previously submitted a Declaration under U.S.C. § 1.131 from Nicholas H. Heintz, a co-inventor of the instant application. The Examiner has objected to the Declaration because there were no original exhibits provided therewith. The Examiner states that the

sequences provided by Applicants are "results" and are thus insufficient to perfect the Declaration.

Applicants are in the process of preparing a substitute Declaration that will more fully elaborate the experimental details that support the discovery of the RIP60 sequences. A draft of this Declaration is provided herewith as Appendix B. This draft Declaration describes the experimental design and results leading to the discovery of the RIP60 sequence. This information has been previously provided to the Examiner in various forms including in the Examples section of the specification, in the Dissertation of co-inventor Christopher R. Houchens (submitted as an appendix to the Provisional Patent Application to which priority is claimed), and in the Nucleic Acids Research reference co-authored by the co-inventors that was previously cited in an Information Disclosure Statement. Applicants are in the process of compiling the "exhibits" requested by the Examiner. Once finalized and executed, the Declaration will be forwarded to the Examiner along with any relevant exhibits.

Upon receipt of the final and executed Declaration, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-3, and 8-9 under 35 U.S.C. §102(a) as being anticipated by Sulston et al. (Genome Research, 8(11):1097-1108, 1998).

Rejection under 35 U.S.C. §103(a)

The Examiner has maintained his rejection of claims 1-16 under 35 U.S.C. §103(a) as being unpatentable over Sulston et al. (Genome Research, 8(11):1097-1108, 1998).

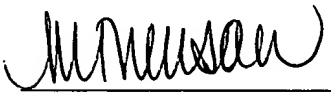
Applicants are preparing a substitute Declaration under U.S.C. § 1.131 from Nicholas N. Heintz with regards to the outstanding U.S.C. § 102 rejection.

Once the final and executed Declaration is received, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-6 and 8-16 under 35 U.S.C. §103(a) as being unpatentable over Sulston et al. (Genome Research, 8(11):1097-1108, 1998).

Summary

If the Examiner has any questions and believes that a telephone conference with Applicants' representative would prove helpful in expediting the prosecution of this application, the Examiner is urged to call the undersigned at (617) 720-3500 (ext. 266).

Respectfully submitted,
Nicholas H. Heintz and
Christopher R. Houchens, Applicant(s)



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Attorney's Docket No.: V00139.70038.US
Date: January 2, 2003
x01.02.03

APPENDIX A:

MARKED-UP CLAIMS

Please amend the claims as follows:

1. (Thrice Amended) An isolated nucleic acid molecule, comprising a nucleic acid molecule selected from the group consisting of

(a) a nucleic acid molecule which hybridizes under stringent conditions to a molecule consisting of a nucleic acid of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:50 and which codes for a polypeptide having a RIP60 activity selected from the group consisting of DNA binding, protein multimerization, and nucleic acid looping,

(b) a nucleic acid molecule that differs from the nucleic acid molecule of (a) in codon sequence due to the degeneracy of the genetic code, and

(c) complements of (a) or (b),

wherein the stringent conditions are hybridization at 65°C in hybridization buffer (3.5x SSC, 0.02% Ficoll, 0.02% polyvinyl pyrolidone, 0.02% Bovine Serum Albumin, 2.5mM NaH_2PO_4 (pH7), 0.5% SDS, 2mM EDTA); wherein SSC is 0.15M sodium chloride/0.015M sodium citrate, pH7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid.

6. (Thrice Amended) An isolated nucleic acid molecule selected from the group consisting of

(a) a fragment of nucleic acid molecule of SEQ ID NO:1 having a length of at least 8 nucleotides, and

(b) complements of (a).

8. (Twice Amended) The isolated nucleic acid molecule of claim 6, wherein the fragment has a size selected from the group consisting of at least: [8 nucleotides,] 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20 nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, and 200 nucleotides.

ATTORNEY'S DOCKET NO.: V00139.70038.US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Nicholas H. Heintz and Christopher R. Houchens
Serial No.:	09/477,392
Conf. No.:	9183
Filed:	January 4, 2000
For:	RIP60 NUCLEIC ACID AND POLYPEPTIDE SEQUENCES AND USES THEREFOR
Examiner:	Robert A. Zeman
Art Unit:	1645

COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

DECLARATION OF NICHOLAS H. HEINTZ, Ph.D. UNDER 37 C.F.R. § 1.131

Sir:

I, Nicholas H. Heintz, declare that:

1. I am an inventor of the above-identified patent application. I make this declaration in support of that application and in response to the Office Action (Paper No. 20) dated July 2, 2002.

2. The purpose of this declaration is to establish reduction to practice of the claimed invention in a WTO member country prior to September 1, 1998, the date of deposit with GenBank of the sequence having Accession Number AC005586, by Sulston et al. This sequence was cited by the Examiner in the above-identified Office Action.

3. I previously submitted a Declaration in support of the above-identified application, which included a copy of the nucleic acid sequence of RIP60 in my possession prior to September 1, 1998, as Exhibit 1.

4. The following process was used by me and Christopher R. Houchens (co-inventor) to discover the nucleotide sequence of RIP60. These experimental procedures are described in the specification of the instant application, in the thesis of Christopher R. Houchens submitted to the

University of Vermont on October 1998 (and submitted to the U.S. Patent Office with the Provisional Patent Application to which the present application claims priority, and in an Information Disclosure Statement submitted on April 11, 2000 (reference CAV)), and in Nucleic Acids Research, Vol. 28, No. 2, pages 57-581 (2000) (submitted to the U.S. Patent Office in an Information Disclosure Statement dated July 12, 2000 (reference CBT).

a. One Hybrid Screen for RIP60.

All oligonucleotides used as probes or primers were synthesized and purified by a combination of denaturing gel electrophoresis and gel elution. Plasmid pBM2389 contains a histidine reporter gene regulated by an enhancerless $P_{GAL1\text{-}UAS}$ promoter (Liu, J., et al, (1993) Meth. Enzymol. 6, 1-13). pBM2389 contains a TRP1 selectable marker and CEN/ARS sequences for plasmid maintenance. Plasmid pJL638 contains a lacZ reporter gene that also is regulated by an enhancerless $P_{Gal1\text{-}uasA}$ promoter (Li, J. J., and Herskowitz, I. (1993) Science 262, 1870-1874). pJL638 contains a URA3 selectable marker but lacks a yeast origin to facilitate chromosomal integration. The pACT expression library contains random human B-cell cDNAs fused to sequences encoding the GAL4 activation domain under the control of an constitutive ADH promoter (Durfee, T., et al, (1993) Genes Dev. 7, 555-559). The vector pACT contains a selectable LEU2 marker and the 2μ origin of replication. Two oligonucleotides representing the downstream RIP60-binding site (OCH7 and OCH8) were annealed, multimerized by ligation, and cloned into the Bam HI site located upstream of the HIS3 reporter gene in pBM2389. Clone pCH14 contains eight repeats of OCH7/OCH8 at the Bam HI site of pBM2389. Five tandem repeats of OCH7/OCH8 (5x-DSR) were removed from pCH14 as a Bam HI/Bgl II fragment and inserted into the Bam HI site of pBM2389 to generate pCH25. The TRP1 marker gene was removed from pCH25 as a Nco I fragment and replaced with the ADE2 marker from pADE2 to generate pCH47. The 5x-DSR fragment was cloned into the Bgl II site located upstream of the lacZ reporter gene in pJL638 to generate pCH33. Fragment E, which contains the downstream RIP60 binding site and surrounding bent DNA sequences (nucleotides 3382-3536 in Caddle, M. S., et al, (1990) J. Mol. Biol. 211, 19-33), was amplified by PCR cloned into the Bam HI and Bgl II sites of pUC19 to generate pUC/E. Fragment E was removed from pUC/E as a Bam HI/Bgl II fragment and inserted into the Bgl II site of pJL638 to generate pCH36. pJL638, pCH33, and pCH36 were each linearized at the Stu I site located in the URA3 marker and integrated at the

URA3 gene in yeast strain GGY1 (*MATα Δgal80 Δura3 leu2 his3 ade2 tyr*) by homologous recombination to generate yeast strains YCH3, YCH4, and YCH5, respectively. Integration of the lacZ reporter plasmids were confirmed by Southern blot analysis. YCH4 was transformed with pCH47 to generate the yeast one hybrid reporter strain, YCH4/pCH47.

YEPD (rich media) and SD (synthetic dropout media) were prepared as described (Gutherie, C., and Fink, G. R. (1991) Guide to Yeast Genetics and Molecular Biology, Academic Press, San Diego, CA). High efficiency yeast transformations were performed by the method of Scheistel and Geitz (Schiestl, R. H., and Gietz, R. D. (1989) Curr. Genet. 16, 339-346). YCH4/pCH47 was transformed with B-cell pACT library DNA and transformants were selected on SD plates lacking histidine, adenine, and leucine. Histidine prototrophs from the transformation (1.9×10^7 total) were assayed for β-galactosidase production (Breeden, L., and Nasmyth, K. (1985) Cold Spring Harb. Symp. Quant. Biol. 50, 643-650) on Protran nitrocellulose filters (Schleicher and Schuell). Transformants which tested positive for lacZ expression were isolated on SD plates lacking leucine and retested for β-galactosidase production. pACT plasmids were isolated from lacZ-positive transformants and purified through bacterial transformation and plasmid isolation. The purified pACT plasmids were retested in YCH4 for beta-galactosidase production and assayed for target sequence specificity in YCH3 and YCH5. Isolated plasmids that tested positive for lacZ expression in YCH4 and/or YCH5, but not YCH3, were sequenced and analyzed in further detail. Clone 146A-1, isolated in the one hybrid screen with YCH4/pCH47, was sequenced on both strands with custom oligonucleotide primers.

b. Isolation of Full-Length RIP60 cDNA.

To isolate full-length clones that encompass the 146A-1 cDNA, XL1-Blue bacterial cells (Stratagene) were infected with a HeLa cDNA library constructed in Lamda Zap (Stratagene) and viral plaques were transferred to Hybond N+ nylon membranes (Amersham). The filters were probed with a random-primed (Life Technologies) radiolabeled probe from the 143A-1 cDNA, which overlaps clone 146A-1. Positive plaques were purified in a secondary screen and pBluescript plasmids excised from isolated Lamda Zap viral particles were sequenced with M13/pUC forward and reverse primers. One clone, pBS-27, which contains overlapping sequence identical to clone 146A-1, was completely sequenced with the following primers: RIP1, OCH32, RIP2, RIP3, RIP4, OCH31, OCH21, OCH23, OCH33, OCH29, OCH24, OCH22,

OCH27, OCH20, and OCH18. The 2.9 kb cDNA of pBS-27 has 129 bp of untranslated 5' sequence, an open reading frame that encodes a 567 amino acid protein of 63 kD (shown in Table 3 of the instant specification), and 1124 bp of 3' non-translated sequence including the poly A tail.

5. In view of the foregoing and the previous Declaration dated February 6, 2002, one of ordinary skill in the art would recognize that I had reduction to practice of the claimed invention in a WTO member country prior to September 1, 1998.

I, the undersigned, declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this document and any patent which may issue from the above-identified patent application.

Date: _____

_____

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